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EXAMINER

KALLIS, RUSSELL

ART UNIT

PAPER NUMBER

1638

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/763,331	MARTIN ET AL.
	Examiner Russell Kallis	Art Unit 1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 04 November 2002.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-5 and 7-20 is/are rejected.

7) Claim(s) 6 is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. _____.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.

4) Interview Summary (PTO-413) Paper No(s) _____.

5) Notice of Informal Patent Application (PTO-152)

6) Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in Paper No. 11 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 7-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims a synthetic fatty acid desaturase gene from an unspecified source comprising a desaturase domain and a cytochrome b₅ domain customized for expression in a plant cytoplasm.

Applicant describes a fatty acid desaturase gene from *Saccharomyces cerevisiae* of SEQ ID NO: 1 and a customized version of the native gene SEQ ID NO: 3 both of which encode the polypeptide of SEQ ID NO: 2.

Applicant does not describe any other synthetic fatty acid desaturase gene from an unspecified source comprising a desaturase domain and a cytochrome b₅ domain customized for expression in a plant cytoplasm.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

Claims 1-5 and 7-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant broadly claims a fatty acid desaturase gene comprising a desaturase domain and a cytochrome b₅ domain optimized for expression in the cytoplasm of plants, under the control of an expression regulatory sequence from a plant gene encoding an ER biosynthetic pathway enzyme, and a method for constructing and testing said optimized bifunctional desaturase/cyt b₅ gene for function in *Saccharomyces cerevisiae*.

Applicant teaches the optimization of the OLE1 nucleic acid sequence of SEQ ID NO: 1 modified to SEQ ID NO: 3 both of which encode SEQ ID NO: 2 for optimal expression in *Arabidopsis* (Example 1 pages 38-41); vacuum infiltration of *Arabidopsis* with the optimized

OLE1 gene *pl-ole1* from *Saccharomyces cerevisiae* (Example 2); prophetic alteration of amino acids of the coding sequence of the OLE1 fatty acid desaturase for increasing catalytic activity of the enzyme and transposition of elements, i.e. the N and C termini, from the *Arabidopsis* FAD2 gene in the coding sequence of the OLE1 fatty acid desaturase for improving modified OLE1 gene expression in a plant (Examples 3 and 4).

Applicant does not teach any other fatty acid desaturase sequence comprising a desaturase domain and a cytochrome b₅ domain optimized for expression in the cytoplasm of plants other than SEQ ID NO: 3.

The design of synthetic genes for increased expression in plants can be a costly and time consuming process of building error free sequences that require the complete resynthesis of the sequence. The use of time and therefore cost consuming techniques such as PCR site directed mutagenesis are necessary for the correction of errors that will inevitably arise during the resynthesis of the gene (Mazier M. *et al.* Biotechnology Annual Review, 1997, pp.313-347 on page 326 lines 12-16 and lines 27-34). The different modifications of the polypeptide will require vigilant screening for point mutations to isolate correct clones. This unpredictable phenomenon seems to be dependent upon the nature of the fragments themselves (Iannocone R. *et al.* Plant Molecular Biology, 1997, Vol. 34, pp. 485-496 on page 490 column 1, lines 17-37). The completed and functionally resynthesized genes encoding the same protein as the wild type gene must be tested for expression in plants (page 491 column 2, lines 5-13 and Abstract lines 12-15).

Given the lack of guidance for making any other non-exemplified optimized or customized fatty acid desaturase genes, comprising a desaturase domain and a cytochrome b₅ domain, that would increase gene expression in plants, the breadth of the claims, and given the

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unpredictability in the art, undue trial and error experimentation would be needed by one skilled in the art to isolate a multitude of non-exemplified optimized fatty acid desaturase genes, or to evaluate the ability of a multitude of non-exemplified optimized fatty acid desaturase genes genes to increase gene expression in a multitude of transformed plant species. Therefore, the invention is not enabled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5 and 7-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitchell A. *et al.* J. of Biol. Chem., December 15, 1995; vol. 270, No. 50; pp. 29766-29772 in view of Fischhoff D. *et al.* U.S. Patent 5,500,365 published March 19, 1996.

Applicant broadly claims a fatty acid desaturase gene comprising a desaturase domain and a cytochrome b₅ domain optimized for expression in the cytoplasm of plants, under the control of an expression regulatory sequence from a plant gene encoding an ER biosynthetic pathway enzyme, and a method for constructing and testing the optimized the said bifunctional desaturase/cyt b₅ gene for function in *Saccharomyces cerevisiae*.

Mitchell teaches the OLE1 gene of *Saccharomyces cerevisiae*, a delta-9 fatty acid desaturase with a cytochrome b₅ domain (Abstract, lines 22-32), and complementation with the OLE1 gene of an OLE1 disrupted (delta-9 deficient) mutant in yeast and a yeast OLE1/cytochrome b₅ disrupted yeast double mutant to test the bifunctional nature of the polypeptide

encoded by the OLE1 gene (page 29769 column 1, lines 1-17). The reference also teaches the inherent placement of a heterologous cytochrome b₅ domain thus teaching what the replacement of the native cytochrome b₅ domain should be.

Mitchell does not teach customizing the OLE1 gene for expression in a dicot or monocot plant, wherein the customization comprises modifications to the sequence that would increase expression in the plant cytoplasm by optimizing codon usage, and eliminating putative intron splice sites, plant polyadenylation signals, termination sequences, or hairpin sequences.

Fischhoff teaches optimization of *B.t. tenebrionis* gene sequence for expression and significantly higher levels of expression in transformed plants when compared to non-optimized *B.t.* gene expression in transformed dicot plants tobacco, tomato, and potato (Example 5 column 34 lines 1-53), and a transformed monocot plant corn (Example 8 column 37, lines 34-40); and the optimizations available to one of skill in the art for increasing the expression of a nucleic acid sequence (columns 1-6; column 10, lines 53-62; and columns 11-12). Fischhoff also suggests the optimization of any transgene for increased expression in transformed plants (column 1, lines 10-22; column 6, lines 30-33).

It would have been obvious at the time of Applicant's invention to modify the invention of Mitchell to comprise a fatty acid desaturase gene comprising a desaturase domain and a cytochrome b₅ domain optimized for expression in the cytoplasm of plants using the method for optimizing genes for expression in plants as taught and suggested by Fischhoff. One of skill in the art would have been motivated by the knowledge common in the art that the fatty acid biosynthesis gene comprising a desaturase domain and a cytochrome b₅ domain optimized for expression in the cytoplasm of plants is a valuable tool for genetic engineering of plants and the

success of Fischoff in increasing gene expression in plants transformed with optimized coding regions, and that one would have had a reasonable expectation of success of expressing genes in transformed plants and plant cells. The choice of a promoter or regulatory region of a gene encoding an ER biosynthetic enzyme to express the fatty acid desaturase gene would have been an obvious design choice.

Claims 1-5 and 7-20 are rejected.

Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the legal analyst, Tiffany Tabb, whose telephone number is (703) 605-1238.

Russell Kallis Ph.D.
January 8, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP 1638

